DRAFTSMAN

SUBCLASS



1/3

CATGGTAGACGGCTGCCCGGAGGGACCACGCGTCTGAGACCGGCGATCGGACCGCCAAAACCATGGGTAGCAATCGGGGCCGCAAG TCTTGCTCTCCTCATGGCTGGCTTGCTGGTGTGGCACTTCCATTATCGGAATGTGCGGGTTCAAAAAGTCTTCAATGGCCATCTG GCTGAAGCTGCTGTACAATGAAGTCCCTGTCCTGGGTCCCTACCACAAGAAGTCGGCTGTAACTGCCTTCAGTGAGGGCAGTGTCA TCGCCTACTACTGGTCAGAGTTCAGCATCCCCCCACACCTGGCAGAAGAGGTTGATCGCGCCCATGGCTGTGGAGCGAGTTGTAACA $\tt TTGCCACCCGAGCACGGGCACTGAAATCCTTCGTGCTAACATCTGTGGTGGCCTTCCCCATTGACCCCAGAATGCTGCAGAGGAC$ TCAGGACAACAGCTGCAGTTTTGCCCTGCATGCCCATGGTGCAGCAGTGACACGCTTCACTACCCCTGGCTTCCCCAACAGTCCCT CACCTTCTCACCCTCCTACAACCTGACTTTCCTCCTCCCAGAACGTCTTCCTTGTCACGCTGATAACCAATACTGACCGGCGAC A'ICCTGGCTTTGAGGCCACTTTCTTCCAGCTGCCCAAGATGAGCAGCTGTGGCGGCTTTTTGAGTGACACCCAAGGGACATTTAGC AGCCCCTACTATCCAGGCCACTACCCGCCCAACATCAACTGCACATGGAATATCAAGGTGCCCAACAACCGGAACGTGAAGGTGCG CTTCAAACTCTTCTATCTGGTGGACCCCAACGTACCAGTGGGCTCCTGCACCAAGGACTATGTGGAGATCAACGGGGAGAAGTACT GCGGTGAGAGGTCCCAGTTTGTGGTGAGCAGCAACAGCAGCAGATTACAGTCCACTTCCATTCTGATCACTCGTACACGGACACC GGGTTCCTAGCTGAGTACCTCTCCTACGACTCCAACGACCCGTGCCCAGGGATGTTCATGTGCAAGACTGGACGGTGCATCCGAAA GCAAAAACCAGTTCTGCAAGCCCCTCTTCTGGGTCTGTGACAGTGTCAACGACTGTGGGGACGGAAGTGACGAGGAGGGCTGCAGC TGTCCTGCTGGGAGTTTCAAGTGTTCCAATGGGAAGTGTCTCCCTCAGAGCCAGAAGTGTAATGGGAAGGACAACTGTGGAGATGG AGGGCAACCCTGAGTGTGATGGGAAGACGGACTGTAGCGATGGCTCCGATGAGAAAAACTGTGACTGTGGGCTGCGATCCTTTACC AAACAGGCTCGCGTGGTTGGTGGCACGAATGCGGACGAGGGGCGAGTGGCCCTGGCAGGTGAGCCTCCACGCCCTGGGCCAGGGCCA ACTACACGATGTGGACGGCCTTCCTGGGTCTGCTGGACCAGAGCAAGCGCAGTGCCTCTGGGGTGCAGGAGCTGAAGCTCAAACGT ATCATCACCCACCCTTCCTTCAATGATTTCACCTTCGACTATGACATCGCCTTGCTGGAGCTGGAGAAGTCGGTGGAGTACAGCAC CGTCGTGCGCCCCATCTGCCTGATGCTACCCATGTCTTCCCTGCTGGCAAGGCCATCTGGGTCACAGGCTGGGGGCACACAA AAGAGGGAGGTACCGGAGCGCTGATCCTGCAGAAGGGTGAGATCCGTGTCATCAACCAGACCACCTGTGAGGACCTCATGCCGCAG CAGATCACCCCACGAATGATGTGTGTGGGGTTTCCTCAGTGGGGGTGTGGACTCCTGCCAGGGTGACTCTGGTGGCCCCTTGTCAAG $\tt CGCGGAGAAGATGGGCGAATGTTCCAGGCTGGTGTGAGCTGGGGTGAAGGCTGCGCTCAGAGGAACAAGCCAGGCGTGTACA$ TGTGAACTGCATCCTTAGGACTCAGAGTTCTTCCAAAGTGGGACCCCCTCAAGAGTTGGAGAGAACTTGCGTGCTAGCGGCCCA GCCTGGGGGCAAGGGTTTGATGGCAGCCTTCCCCCTCTAGCCCTGAGCTGGGTGAAGATGATGCTGTCCCGGAGAGCTGCTTCCAA CTGTCATTGAGCTCCCGGGAGCCCTATGGGAGGAGGGGCTCAGGGTCACTCTTTTCAGGAAGCGCCAGCCCTAGGAACCCCAGAAA AAAAAAAAA (SEQ ID NO:1)

> MGSNRGRKAGGGSQDFGAGLKYNSRLENMNGFEEGVEFLPANNA KKVEKRGPRRWVVLVAVLFSFLLLSLMAGLLVWHFHYRNVRVQKVFNGHLRITNEIFL DAYENSTSTEFISLASOVKEALKLLYNEVPVLGPYHKKSAVTAFSEGSVIAYYWSEFS IPPHLAEEVDRAMAVERVVTLPPRARALKSFVLTSVVAFPIDPRMLQRTQDNSCSFAL HAHGAAVTRFTTPGFPNSPYPAHARCQWVLRGDADSVLSLTFRSFDVAPCDEHGSDLV TVYDSLSPMEPHAVVRLCGTFSPSYNLTFLSSQNVFLVTLITNTDRRHPGFEATFFQL PKMSSCGGFLSDTQGTFSSPYYPGHYPPNINCTWNIKVPNNRNVKVRFKLFYLVDPNV PVGSCTKDYVEINGEKYCGERSQFVVSSNSSKITVHFHSDHSYTDTGFLAEYLSYDSN DPCPGMFMCKTGRCIRKELRCDGWADCPDYSDERYCRCNATHQFTCKNQFCKPLFWVC DSVNDCGDGSDEEGCSCPAGSFKCSNGKCLPQSQKCNGKDNCGDGSDEASCDSVNVVS $\verb|CTKYTYRCQNGLCLSKGNPECDGKTDCSDGSDEKNCDCGLRSFTKQARVVGGTNADEG|$ EWPWOVSLHALGOGHLCGASLISPDWLVSAAHCFQDDKNFKYSDYTMWTAFLGLLDQS KRSASGVQELKLKRIITHPSFNDFTFDYDIALLELEKSVEYSTVVRPICLPDATHVFP AGKAIWVTGWGHTKEGGTGALILQKGEIRVINQTTCEDLMPQQITPRMMCVGFLSGGV DSCQGDSGGPLSSAEKDGRMFQAGVVSWGEGCAQRNKPGVYTRLPVVRDWIKEHTGV (SEQ ID NO:2)

FIGURE 1

'n IT -2 := 1.4 ---<u>...</u> Ü ::å:

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<u>underlined</u> = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

CATGGTAGACGGCTGCCCGGAGGGACCACGCGTCTGAGACCGGCGATCGGACCGCCAAAA CCATGGGTAGCAATCGGGGCCGCAAGGCCGGAGGGGGCTCTCAGGACTTCGGCGCGGGAC ${ t TCAAGTACAACTCCCGGCTAGAGAACATGAATGGCTTTGAGGAGGGTGTGGAGTTCCTGC}$ ATTATCGGAATGTGCGGGTTCAAAAAGTCTTCAATGGCCATCTGAGGATCACAAATGAGA TGAAGGAGGCGCTGAAGCTGCTGTACAATGAAGTCCCTGTCCTGGGTCCCTACCACAAGA AGTCGGCTGTAACTGCCTTCAGTGAGGGCAGTGTCATCGCCTACTACTGGTCAGAGTTCA GCATCCCCCACACCTGGCAGAAGAGGTTGATCGCGCCATGGCTGTGGAGCGAGTTGTAA CATTGCCACCCGAGCACGGGCACTGAAATCCTTCGTGCTAACATCTGTGGTGGCCTTCCCCCATTGACCCCAGAATGCTGCAGAGGACTCAGGACAACAGCTGCAGTTTTTGCCCTGCATG CCCATGGTGCAGCAGTGACACGCTTCACTACCCCTGGCTTCCCCAACAGTCCCTACCCGG CGCATGCCCGCTGCCAGTGGGTCCTGCGGGGGGACGCCGACTCTGTGCTGAGCCTCACCT TCCGAAGCTTTGATGTCGCTCCCTGTGATGAGCATGGCAGTGACCTGGTCACCGTGTATG ATAGCCTGAGCCCCATGGAACCCCACGCTGTGGTGCGGCTGTGTGGCACCTTCTCACCCT CCTACAACCTGACTTTCCTCCTCCCAGAACGTCTTCCTTGTCACGCTGATAACCAATA CTGACCGGCGACATCCTGGCTTTGAGGCCACTTTCTTCCAGCTGCCCAAGATGAGCAGCT GTGGCGGCTTTTTGAGTGACACCCAAGGGACATTTAGCAGCCCCTACTATCCAGGCCACT ACCCGCCCAACATCAACTGCACATGGAATATCAAGGTGCCCAACAACCGGAACGTGAAGG TGCGCTTCAAACTCTTCTATCTGGTGGACCCCAACGTACCAGTGGGCTCCTGCACCAAGG ACTATGTGGAGATCAACGGGGAGAAGTACTGCGGTGAGAGGTCCCAGTTTGTGGTGAGCA GCAACAGCAGCAAGATTACAGTCCACTTCCATTCTGATCACTCGTACACGGACACCGGGT TCCTAGCTGAGTACCTCTCCTACGACTCCAACGACCCGTGCCCAGGGATGTTCATGTGCA AGACTGGACGGTGCATCCGAAAGGAACTGCGCTGCGACGGCTGGGCAGACTGCCCGGATT ATAGTGATGAGCGTTACTGCCGATGCAATGCCACCCACCAGTTCACGTGCAAAAACCAGT TCTGCAAGCCCCTCTTCTGGGTCTGTGACAGTGTCAACGACTGTGGGGACGGAAGTGACG AGGAGGGCTGCAGCTGTCCTGCTGGGAGTTTCAAGTGTTCCAATGGGAAGTGTCTCCCTCAGAGCCAGAAGTGTAATGGGAAGGACAACTGTGGAGATGGCTCTGACGAGGCTTCATGTG ACAGCGTGAATGTCGTCTTTGCACCAAATATACCTACCGCTGCCAAAATGGCCTCTGTC TGAGCAAGGGCAACCCTGAGTGTGATGGGAAGACGGACTGTAGCGATGGCTCCGATGAGA ATGCGGACGAGGGCGAGTGGCCCTGGCAGGTGAGCCTCCACGCCCTGGGCCAGGGCCACT TGTGTGGGGCCTCGCTCATCTCTCCTGACTGGCTGGTCTCTGCAGCTCATTGCTTTCAGG ATGACAAAAATTTCAAGTACTCAGACTACACGATGTGGACGGCCTTCCTGGGTCTGCTGG ACCAGAGCAAGCGCAGTGCCTCTGGGGTGCAGGAGCTGAAGCTCAAACGTATCATCACCC ACCCTTCCTTCAATGATTTCACCTTCGACTATGACATCGCCTTGCTGGAGCTGGAGAAGT CTGCTGGCAAGGCCATCTGGGTCACAGGCTGGGGGCACACAAAAGAGGGAG [GTACCGGA GCGCTGATCCTGCAGAAGGGTGAGATCCGTGTCATCAACCAGACCACCTGTGAGGACCTC ATGCCGCAGCAGATCACCCCACGAATGATGTGTGTGGGTTTCCTCAGTGGGGGTGTGGAC TCCTGC]CAGGGTGACTCTGGTGGCCCCTTGTCAAGCGCGGAGAAAG[ATGGGCGAATGT TCCAGGCTGGTGTGAGCTGGGGTGAAGGCTGCGCTCAGAGGAACAAGCCAGGCGTGT ACACAAGGCTCCCTGTAGTTCGGGACTGGATCAAAGAGCACACTGGGGTATAGCAGCATG GACAGACAGCCGACCACAAACACCCACAGGGATGCCCGACATGCACACCTGGATACAGGA ACTGCATCCTTAGGACTCAGAGTTCTTCCAAAGTGGGACCCCCTCAAGAGTTGGAGAGAG AACTTGCGTGCTAGCGGCCCAGCCTGGGGGCAAGGGTTTGATGGCAGCCTTCCCCCTCTA GCCCTGAGCTGGAGATGATGCTGTCCCGGAGAGCTGCTTCCAACTGTCATTGAGCT CCCGGGAGCCCTATGGGAGGGGGCTCAGGGTCACTCTTTTCAGGAAGCGCCAGCCCTA GGAACCCCAGAAAAGAGTGGTACCTAAGGCTGAAAT] TGTTTTGCTGTTGCCAGGGGTGG

FIGURE 2A





Gene Sequence Structure 2466 bp **Sequence Deleted** 2505 bp Size of full-length cDNA: 3106 bp Targeting Vector* Neo (genomic sequence) Cassette 5' arm 3' arm Construct Number: 2035 5' probe Arm Length: 5': 3.8 kb 3': 1 kb 5'>ATGGGCGAATGTTCCAGGCTG 5'>TTCCCCATTGAGACTGGCTTA GTGTGGTGGGCTGGGGTGAAGGCT CCCCGGAAGCTGCCTGCCTCAGTC TCCCGCTTCCTGTCTCCCCAGGTA GCGCTCAGAGGAACAAGCCAGGCG TGTACACAAGGCTCCCTGTAGTTC CCGGAGCGCTGATCCTGCAGAAGG GGGACTGGATCAAAGAGCACACTG GTGAGATCCGTGTCATCAACCAGA Targeting Vector CCACCTGTGAGGACCTCATGCCGC GGGTATAGCAGCATGGACAGACAG **Endogenous Locus** AGCAGATCACCCCACGAATGATGT CCGACCACAAACACCCACAGGGAT GTGTGGGTTTCCTCAGTGGGGGTG GCCCGACATGCACACCTGGATACA * Not drawn to scale TGGACTCCTGC<3' GGAGAGGGACA<3' (SEQ ID NO:3) (SEQ ID NO:4)

FIGURE 2B